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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/993,647	11/27/2001	Bernd Riedl	BAYER 18A	1010

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EXAMINER	
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ART UNIT	PAPER NUMBER
1624	

MAIL DATE	DELIVERY MODE
06/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	Application No. 09/993,647	Applicant(s) RIEDL ET AL.	
	Examiner Deepak Rao	Art Unit 1624	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 5/29/07 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 4 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☒ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *see attached*. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☐ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: _____.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☐ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

/Deepak Rao/
Primary Examiner
Art Unit: 1624

ADVISORY ACTION

This action is in response to the amendment filed on May 29, 2007 in response to the final rejection of January 29, 2007.

Information Disclosure Statement

The information disclosure statements filed May 11, 2007 and May 29, 2007 fail to comply with 37 CFR 1.97(d) because it lacks a statement as specified in 37 CFR 1.97(e). It has been placed in the application file, but the information referred to therein has not been considered. See MPEP § 609 (provided below for convenience):

609 [R-2] **Information Disclosure Statement**
37 CFR 1.97. Filing of information disclosure statement.
(a) In order for an applicant for a patent or for a reissue of a patent to have an information disclosure statement in compliance with § 1.98 considered by the Office during the pendency of the application, the information disclosure statement must satisfy one of paragraphs (b), (c), or (d) of this section.
(b) An information disclosure statement shall be considered by the Office if filed by the applicant within any one of the following time periods:
(1) Within three months of the filing date of a national application other than a continued prosecution application under § 1.53(d);
(2) Within three months of the date of entry of the national stage as set forth in § 1.491 in an international application;
(3) Before the mailing of a first Office action on the merits; or
(4) Before the mailing of a first Office action after the filing of a request for continued examination under § 1.114.
(c) An information disclosure statement shall be considered by the Office if filed after the period specified in paragraph (b) of this section, provided that the information disclosure statement is filed before the mailing date of any of a final action under § 1.113, a notice of allowance under § 1.311, or an action that otherwise closes prosecution in the application, and it is accompanied by one of:
(1) The statement specified in paragraph (e) of this section; or
(2) The fee set forth in § 1.17(p).
(d) An information disclosure statement shall be considered by the Office if filed by the applicant after the period specified in paragraph (c) of this section, provided that the information disclosure statement is filed on or before payment of the issue fee and is accompanied by:
(1) The statement specified in paragraph (e) of this section; and
(2) The fee set forth in § 1.17(p).
(e) A statement under this section must state either:
(1) That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement; or
(2) That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in § 1.56(c) more than three months prior to the filing of the information disclosure statement.

The amendment filed May 29, 2007 under 37 CFR 1.116 in reply to the final rejection has been considered but is not deemed to place the application in condition for allowance and **will not be entered** because:

1. The amendment is not deemed to overcome the rejection under 35 U.S.C. 112, first paragraph of claims 74, 81, 87, 93, 99-103, 105-114 and 117. The reasons provided in the previous office action are incorporated here by reference. Applicant cites *In re Marzocchi*, 169 USPQ 367, and argues that 'there is no evidence that the claimed methods are not enabled'. However, the examiner has provided both reasoning including the nature of the invention which is directed to an unpredictable art, citation of case law as well as relevant publication to support the reason for the rejection. Applicant has not identified any state of the art references that clearly establish correlation between the assays employed in the specification and clinical efficacy for the treatment of the claimed diseases. Where the utility is unusual or difficult to treat or speculative, the examiner has authority to require evidence that tests relied on are reasonably predictive of *in vivo* efficacy by those skilled in the art.

Applicant argues that 'no evidence has been presented to refute the findings or conclusions made in the publications'. However, contrary to applicant's arguments, the state of the art references Kolch and/or Monia do not establish a therapeutic method for the treatment of all types of solid tumors, carcinomas, myeloid disorders or adenomas generally. As explained in the previous office action, the state of the art is not indicative of the fact that treatment of all types of diseases encompassed by the instant claims are conventional or well known. The cited references are too speculative and invite further research into treatment of cancer diseases. For example, Monia at page 668 provides that "the emergence of novel therapies that specifically

reverse the oncogenic effect of these gene products has generally been slow". Applicant draws attention to additional references that are filed May 29, 2007 in a Information Disclosure Statement. However, this IDS does not comply with 37 CFR 1.97(d) and therefore, the cited references therein are not considered. Thus, contrary to applicant's arguments, the state of the art does not establish that a single therapeutic approach exists for the treatment of the types of diseases within the scope of instant claims.

Further, claim 117 is directed towards 'a method for inhibiting RAF-kinase in a human or mammal' and therefore reaches through to the treatment of all types of diseases associated with RAF-kinase. The findings and conclusions in the cited publications with respect to inhibition of RAF kinase and the application of such activity for specific types of cancerous growth. The development of the most efficacious strategy for the treatment of cancers is based on understanding the underlying mechanisms of carcinogenesis. This includes the knowledge that the carcinogenic process is a multi-step, multi-mechanism process and that no two cancers are alike, in spite of some apparent universal characteristics, such as their inability to have growth control, to terminally differentiate, to apoptose abnormally and to have an apparent extended or immortalized life span. Since tumor promotion phase involves multiple mechanisms, there is no existence of a single therapeutic approach. The evidence of record does not disclose any known compounds of similar structure, which have been demonstrated to treat all diseases mediated by raf kinase, or all solid tumors, carcinomas, myeloid disorders or adenomas.

2. The proposed amendment and arguments are not deemed to overcome the rejections under 35 U.S.C. 102(a) of the previous office action. Applicant relies on 132 declarations

executed by Reidl, Dumas, Lowinger and Smith. The declaration, filed after final rejection, requires review and consideration of numerous applications to ascertain the common inventorship or ownership. Further, the declaration does not appear to be an uncontradicted "unequivocal statement" as it is not executed by all the co-inventors, which is required according to MPEP 715.01(c) in order to establish the reference is a publication of applicant's own invention.

3. The provisional obviousness-type double patenting rejection over copending Application No. 10/361,850 (now allowed) continues to be applicable. Applicant has not provided any arguments regarding this rejection. It was previously submitted that 'the rejection is premature as allowable subject matter has not been identified'.

4. The proposed amendment raises new issues that would require further search and/or consideration. The instant claims according to the proposed amendment recite "or a pharmaceutically acceptable salt thereof", which requires further search and/or consideration as the recitation changes the scope of the claims.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Monday-Friday from 8:00am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, can be reached at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Deepak Rao/
Primary Examiner
Art Unit 1624

June 14, 2007